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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/173,463	10/14/1998	MARGARET E. BLACK	240052.429	1873

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EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	PAPER NUMBER
1652	
MAIL DATE	DELIVERY MODE
09/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	09/173,463	BLACK, MARGARET E.	
	Examiner	Art Unit	
	Christian L. Fronda	1652	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 03 July 2007 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-15*.
   Claim(s) withdrawn from consideration: *16-60*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

Continuation of 3. NOTE:
The claims as amended in the amendment date 07/03/2007 would be rejected under rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The recitation of SEQ ID NO: 1 (a nucleotide sequence) does not particularly identify the specific amino acid residues in the Herpesviridae thymidine kinase which are to be mutated. Amending the claims to recite the specific amino acid sequence of the Herpesviridae thymidine kinase to be mutated may help in overcoming the rejection.

Claims 1, 3, 6, 8-11 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Munir et al. in view of Graham et al., Kit et al., Drake et al., Waldman et al., Munch Petersen et al., Balasubramaniam et al., Brown et al., and Donarian et al. In response to the arguments that the examiner's conclusion of obviousness for claims 1, 3, 6, and 8-11 is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The references of Balasubramaniam et al. and Brown et al. teach that the Q substrate binding domain and the DRH binding domain are important in nucleoside binding and that in order to obtain mutants having the desired properties (i.e. increased enzyme activity or greater substrate/analog/prodrug specificity) this region must be modified; and thus, provide a motivation to make the claimed invention. Since recombinant molecular biology and random mutagenesis techniques are well known and predictable in the art, one of ordinary skill in the art at the time the invention was made would have used the random mutagenesis method taught by Munir et al. to randomly mutate the codons encoding these important domains in order to obtain and screen for mutants with enhanced properties such as greater substrate, analog, or prodrug specificity and that such mutants having increased activity toward prodrugs such as ganciclovir.

Claims 12-15 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Esandi et al. in view of Munir et al., Graham et al., Kit et al., and Donarian et al. In response to the arguments regarding claims 12-15 that there is no motivation and expectation of success, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and In re Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Recombinant molecular biology and random mutagenesis techniques are well known and predictable to one of ordinary skill in the art. As stated previously, the Donarian et al. reference teaches that the α fetoprotein promoter (a tissue specific promoter) is suitable in the control of prodrug activating or toxic enzymes in the gene therapy of cancer. Furthermore, thymidine kinase mutants having increased activity toward prodrugs such as ganciclovir are expected to be more effective in the treatment of cancer when these mutants are used in gene therapy as taught by Donarian et al.. Thus, the teachings of the references provide a motivation to make the claimed invention, where one of ordinary skill in the art would have made an expression vector comprising a promoter operably linked to the claimed nucleic acid encoding the claimed Herpesviridae thymidine kinase by inserting the mutated DNA encoding mutant thymidine kinase described above in the rejection of claims 1, 3, 6, 8-11 into the expression vector taught by Esandi et al. in order to express thymidine kinase mutants in cancer cells of specific tissue origin. .

T Saidha

TEKCHAND SAIDHA
PRIMARY EXAMINER